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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,059	STARK ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *5,6,15-17,24-27,43-45,48-51,60-66 and 69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-14,18-23,28-42,46,47,52-59,67 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/GB03/04169.

Claims 1-69 are currently pending.

The preliminary amendment filed on 3/20/2007, amending claims 36-37, and 40 is acknowledged.

Applicant's election with traverse of Group I, Claims 1-14, 18-42, 46-59, ad 67-68, drawn to an isolated polypeptide a serine recombinase, hybrid recombinase mutated at position 101 and a catalytic domain peptide and a DNA binding domain, and a kit and species A protein (TN3 resolvase) and SEQ ID NO: 31 from claim 36 in the response filed on 7/30/2007 and 3/20/2007 is acknowledged.

The traversal is on the ground(s) of Special technical feature for restriction requirement that was applied by the Examiner, was not proper. In the previous Office action, Examiner established lack of unity as follows:

The inventions listed as Groups I - XVII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features because the polynucleotide encoding a polypeptide of Group XII-XV and polypeptide of Group I-XII are each unrelated and chemically distinct entities. The only shared technical feature of these groups is that they all relate to polynucleotide encoding a polypeptide serine recombinase. However, this shared technical feature is not a "special technical feature" as defined by PCT Rule 13.2 as it does not define a contribution over the art. Arnold et al. teach a serine recombinase Tn3 resolvase and a mutant G101S and its corresponding DNA molecule. (Mutants of Tn3 resolvase, which do not require accessory

binding sites for recombination activity, EMBO J. 1999 Mar 1; 18(5): 1407-14, see IDS). Thus, a DNA encoding a serine recombinase protein does not make contribution over the prior art. Therefore, it lacks special technical feature.

Applicants argue that the inventions of Groups I to XII have the same or corresponding technical features and PCT Rule 13.2 defines the expression "special technical feature" to mean those technical features that define a contribution with each of the claimed inventions, considered as a whole, makes over the prior art. Applicants also argue that the special technical feature of the invention recited by the claims of Groups I to XII require, a combination of polymorphisms that define a contribution over the prior art (and the cited reference Arnold *et al.)* as set forth, for example, in the subject matter of claims 1 and 7. Applicants further argue that the International Search Authority found that additional substitutions constituted a single invention for examination purposes. Accordingly, Applicants respectfully request that the claims of Group II to XII be rejoined and examined with Group I.

This is not found persuasive because a special technical feature MUST be a feature present in all claims, for all claims to have unity of invention. The term "special technical feature" means a common feature among the claims, which if that feature is not known then unity of invention exists but if that feature is known, all the claims lack unity of invention. As discussed in the previous office action, Arnold et al. teach a mutant serine recombinase having a mutation at G101, which is the "special technical feature" of all the claims of instant application, which is known. Therefore, all the claims lack unity of invention. In addition, examination in the national phase is not bound by the international phase findings.

As restriction is clearly permissible even among related inventions as defined in MPEP

808 and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 4-5, 15-17, 24-27, 43-45, 48-51, 60-66 and 69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-3, 6-14, 18-23, 28-42, 46-47, 52-59 and 67-68 are under consideration and will be examined herein.

Priority

Acknowledgement is made of applicants claim for foreign priority of United Kingdom 0222229.7 filed on 9/25/2002 and priority date is granted because of having support of the claimed invention and the document is in English language.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 10/8/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is considered by the examiner. The signed copy of IDS is enclosed herewith.

Drawings

Drawings submitted on 3/24/2005 are objected by the Examiner for the recitation of the nucleic acid and protein sequences without appropriate sequence identifiers i.e. SEQ ID NOs.

Examiner urges the applicants to provide sequence identifiers in response to this Office action. See particularly 37 CFR 1.821(d).

Non-compliance of Sequence Rule

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that in drawings, Figure 1 recites the amino acid sequence without a corresponding sequence identifier recited. See particularly 37 CFR 1.821(d).

Claim Objections

Claims 2-4, and 7-14 are objected to because of the recitation "A recombinase", which depends from the claim 1 directly or indirectly, which should be "The recombinase". Appropriate correction is required.

Claims 18-23, and 28-42 are objected to because of the recitation "A hybrid recombinase", which depends from the claim 18 directly or indirectly, which should be "The hybrid recombinase". Appropriate correction is required.

Claims 47, and 52-59 are objected to because of the recitation "A catalytic domain", which depends from the claim 46 directly or indirectly, which should be "The catalytic domain". Appropriate correction is required.

Claim 8 is objected to in the recitation of "comprising a one or more mutations", which should be "comprising one or more mutations". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 8-11 and 53-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 8-11 and 53-56 recite "1,3 or 1,2 or 2,3 interface", which is unclear to the Examiner. The specification does not define what does the phrase mean? "Interface" meaning is comprehensible but 1,2 or 2,3 interface is ambiguous and confusing.

Claims 18-23, 28-38 and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 is indefinite in the recitation "said catalysing" lacks antecedent basis and claim 18 does not recite "catalysing" before said phrase in claim 18.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 7-14, 18-22, 28-42, 46-47, 52-59 and 67-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 7-14, 18-22, 28-42, 46-47, 52-59 and 67-68 are directed to a genus of serine recombinase comprising a catalytic domain and a DNA binding domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of any TN3 resolvase or any hybrid recombinase comprising a catalytic domain from any serine recombinase, and DNA binding domain of any Zif268 protein, wherein said hybrid recombinase is capable of binding nucleic acid by said DNA binding domain and catalyzing recombination of said DNA or a catalytic domain of any serine recombinase which has been mutated at G101 or at a position corresponding to G101 of any Tn3 resolvase and a kit comprising any serine recombinase or any hybrid recombinase.

As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the structure of only few representative species of such recombinase proteins and catalytic domain. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding the polypeptide having recombination

activity. Given this lack of description of representative species encompassed by the genus of proteins of the claim and used to make a kit, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-4, 7-14, 18-22, 28-42, 46-47, 52-59 and 67-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide a serine recombinase Tn3 resolvase from E. coli comprising a catalytic domain and a DNA binding domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of a Tn3 resolvase from E. coli or a hybrid recombinase comprising a catalytic domain of Tn3 resolvase from E. coli, and DNA binding domain of a Zif268 protein, wherein said hybrid recombinase is capable of binding nucleic acid by said DNA binding domain and catalyzing recombination of said DNA or a catalytic domain of a serine recombinase Tn3 resolvase which has been mutated at G101 or at a position corresponding to G101 of a Tn3 resolvase from E. coli and a kit comprising a serine recombinase of Tn3 resolvase or a hybrid recombinase, does not reasonably provide enablement for a polypeptide of any serine recombinase from any source comprising any catalytic domain and any DNA binding domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of any Tn3 resolvase from any source or a hybrid recombinase comprising any catalytic domain and any DNA binding domain, wherein said hybrid recombinase is capable of binding nucleic acid by said DNA binding domain and catalyzing recombination of said DNA or any catalytic domain of any serine recombinase and a kit comprising any serine recombinase or a hybrid recombinase comprising any serine

recombinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-4, 7-14, 18-22, 28-42, 46-47, 52-59 and 67-68 are so broad as to encompass a polypeptide of any serine recombinase from any source comprising any catalytic domain and any DNA binding domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of any Tn3 resolvase from any source or a hybrid recombinase comprising any catalytic domain and any DNA binding domain, wherein said hybrid recombinase is capable of binding nucleic acid by said DNA binding domain and catalyzing recombination of said DNA or any catalytic domain of any serine recombinase and a kit comprising any serine recombinase or a hybrid recombinase comprising any serine recombinase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of serine recombinase broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one serine recombinase i.e. Tn3 resolvase from E. coli.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims,

and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions.

The specification does not support the broad scope of the claims which encompass a polypeptide of any serine recombinase from any source comprising any catalytic domain and any DNA binding domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of any Tn3 resolvase from any source or a hybrid recombinase comprising any catalytic domain and any DNA binding domain, wherein said hybrid recombinase is capable of binding nucleic acid by said DNA binding domain and catalyzing recombination of said DNA or any catalytic domain of any serine recombinase and a kit comprising any serine recombinase or a hybrid recombinase comprising any serine recombinase because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting recombinase activity; (B) the general tolerance of recombinase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any serine recombinase amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a polypeptide of any serine recombinase from any source

comprising any catalytic domain and any DNA binding domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of any Tn3 resolvase from any source or a hybrid recombinase comprising any catalytic domain and any DNA binding domain, wherein said hybrid recombinase is capable of binding nucleic acid by said DNA binding domain and catalyzing recombination of said DNA or any catalytic domain of any serine recombinase and a kit comprising any serine recombinase or a hybrid recombinase comprising any serine recombinase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any serine recombinase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 7-8, 10-11, 14, 46-47, 52-53, 55-56, and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Arnold et al. (Mutants of Tn3 resolvase which do not require accessory binding sites for recombination activity, EMBO J. 1999 Mar 1; 18(5): 1407-14, see IDS). Instant claims directed to a mutant serine recombinase Tn3 resolvase comprising a mutation at position G101, wherein the mutation is G101S, additional mutations including

E124Q, D102Y, M103I, interface, catalytic domain of a serine recombinase comprising a mutation of G101S, further comprising additional mutations including E124Q, wherein catalytic domain comprises an interface including mutation of at positions M 103I. Arnold et al. teach a mutant serine recombinase Tn3 resolvase comprising a mutation at position G101, wherein the mutation is G101S. Arnold et al. also teach additional mutations including E124Q, D102Y, M103I, which are located on the surface of the interface of a serine recombinase. Since, applicants define mutation at position E124 in the specification, which is at 1,2 interface of a serine recombinase, mutation at position E124 as E124Q as taught by Arnold et al. would inherently be in the 1,2 interface of a serine recombinase. Arnold et al. further teach a catalytic domain of a serine recombinase comprising a mutation of G101S, and further comprising additional mutations including E124Q, D102Y, wherein catalytic domain also comprises an interface including mutation of at positions M 103I. Therefore, Arnold et al. anticipate Claims 1-2, 7, 10-11, 14, 46-47, 52-53, 55-56, and 59 of the instant application.

Claims 1-4, 7-12, 14, 46-47 and 52-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Sarkis et al. (A model for the gamma delta resolvase synaptic complex, Mol Cell. 2001 Sep;8(3): 623-31, see IDS). Instant claims directed to a mutant serine recombinase Tn3 resolvase comprising a mutation G101S, and further comprising a mutation Q105L, having one or more mutations at the 2,3 interface R2A and E56K and mutations at positions including E124Q, D102Y, M103I and a catalytic domain comprising 2,3 interface comprising mutations including M103I. Sarkis et al. teach a mutant serine recombinase Tn3 resolvase comprising a mutation at position G101, wherein the mutation is G101S a mutant serine recombinase Tn3

resolvase, and further comprising a mutation Q105L, having one or more mutations at the 2,3 interface R2A and E56K. Sarkis et al. also teach catalytic domain of a serine recombinase comprising a mutation of G101S, and further comprising additional mutations including E124Q, D102Y, wherein catalytic domain also comprises an 2,3 interface including mutation at position M 103I and DNA binding domain. Therefore, Sarkis et al. anticipate Claims 1, 3-4, 7-12, 14, 46-47 and 52-59 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-35, 38-39, 41-42, 57 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arnold et al. (Mutants of Tn3 resolvase which do not require accessory

binding sites for recombination activity, EMBO J. 1999 Mar 1; 18(5): 1407-14), Sarkis et al. (A model for the gamma delta resolvase synaptic complex, Mol Cell. 2001 Sep;8(3): 623-31, in view of Jamieson et al. (A zinc finger directory for high-affinity DNA recognition. Proc Natl Acad Sci U S A. 1996 Nov 12; 93(23): 12834-9). Instant claims are directed to a hybrid or chimeric recombinase i.e. Tn3 resolvase, wherein the catalytic domain is from Tn3 resolvase of E. coli and a heterologous DNA binding domain of Zif268 and a linker sequence comprises SEQ ID NO: 31 and a kit comprising said hybrid recombinase.

Arnold et al. teach a mutant serine recombinase Tn3 resolvase comprising a mutation at position G101, wherein the mutation is G101S. Arnold et al. also teach additional mutations including E124Q, D102Y, M103I, which are located on the surface of the interface of a serine recombinase. Since, applicants define mutation at position E124 in the specification, which is at 1,2 interface of a serine recombinase, mutation at position E124 as E124Q as taught by Arnold et al. would inherently be in the 1,2 interface of a serine recombinase. Arnold et al. further teach a catalytic domain of a serine recombinase comprising a mutation of G101S, and further comprising additional mutations including E124Q, D102Y, wherein catalytic domain also comprises an interface including mutation of at positions M 103I. The catalytic domain of Arnold et al. and the instant application is the same. Therefore, the length (amino acid 1-148) of the catalytic domain (claims 31-35) of Arnold et al. would be the same as the instant application. Sarkis et al. teach a catalytic domain having all the mutations of claim 57. Arnold et al. do not teach a hybrid or chimeric or recombinant recombinase of Tn3 resolvase having a heterologous DNA binding domain, a linker sequence and a kit comprising said hybrid recombinase.

Sarkis et al. teach a mutant serine recombinase Tn3 resolvase comprising a mutation at position G101, wherein the mutation is G101S a mutant serine recombinase Tn3 resolvase, and further comprising a mutation Q105L, having one or more mutations at the 2,3 interface R2A and E56K. Sarkis et al. also teach catalytic domain of a serine recombinase comprising a mutation of G101S, and further comprising additional mutations including E124Q, D102Y, wherein catalytic domain also comprises an 2,3 interface including mutation at position M 103I and DNA binding domain. The catalytic domain of Sarkis et al. and the instant application is the same. Therefore, the length (amino acid 1-148) of the catalytic domain (claims 31-35) of Sarkis et al. would be the same as the instant application. Sarkis et al. teach a catalytic domain having all the mutations of claim 57. Sarkis et al. do not teach a hybrid or chimeric or recombinant recombinase of Tn3 resolvase having a heterologous DNA binding domain or a linker sequence and a kit comprising said hybrid recombinase.

Jamieson et al. teach a DNA binding domain Zif268, a murine transcription factor egr-1 family, which is a Zinc finger DNA binding domain having the ability to bind DNA molecule comprising G-rich region.

By combining the teachings of Arnold et al., Sarkis et al., and Jamieson et al. it would have been obvious to one of ordinary skill in the art at the time of the invention was made to replace the DNA binding domain of Tn3 resolvase of Arnold et al. and Sarkis et al. with DNA binding domain of Jamieson et al. to make a hybrid or chimeric or recombinant recombinase because the DNA binding domain of Jamieson et al. has the affinity to bind G-rich region of a DNA sequence in order to direct the recombinase activity to a desired new site. Since, DNA binding domain are present in both transcription factors and recombinase, both of which need to

bind specific DNA sequence for exerting their functional activities by catalytic domain of recombinase for excising DNA and recombination, or recruiting RNA polymerase for the activation of transcription. One of ordinary skilled in the artisan would be expected to make a kit comprising said hybrid recombinase for convenience for the user. It would have been obvious to one of ordinary skill in the art to insert a linker between catalytic domain of Arnold et al. and Sarkis et al. and DNA binding domain of Jamieson et al. to make a recombinant protein, which is widely used in the art to make the recombinant protein express efficiently and function properly.

One of ordinary skill in the art would have been motivated to use Zif268 DNA binding domain instead of Tn3 resolvase DNA binding domain for specifically recombination of G-rich region.

One of ordinary skill in the art would have a reasonable expectation of success because making a hybrid or chimeric or recombinant protein is well known in the art.

Therefore, claims 18-35, 38-39, 41-42 and 68 would have been prima *facie* obvious to use one of ordinary skill in the art.

Claim 67 is rejected under 35 U.S.C. 103(a) as being unpatentable over Arnold et al. (Mutants of Tn3 resolvase which do not require accessory binding sites for recombination activity, EMBO J. 1999 Mar 1; 18(5): 1407-14), Sarkis et al. (A model for the gamma delta resolvase synaptic complex, Mol Cell. 2001 Sep;8(3): 623-31, in view of Pati et al. US PGPUB 2004/0091885, publication 5/13/2004, claim priority of 60/070,734 filed on 12/11/1997). Instant claim is directed to a kit comprising serine recombinase i.e. Tn3 resolvase.

Arnold et al. teach a mutant serine recombinase Tn3 resolvase comprising a catalytic domain and DNA binding domain, a mutation at position G101, wherein the mutation is G101S. Arnold et al. also teach additional mutations including E124Q, D102Y, M103I as well as interface. Arnold et al. further teach a catalytic domain of a serine recombinase comprising a mutation of G101S, and further comprising additional mutations including E124Q, wherein catalytic domain comprises an interface including mutation of at positions M 103I. The catalytic domain of Arnold et al. and the instant application is the same. Therefore, the length (amino acid 1-148) of the catalytic domain (claims 31-35) of Arnold et al. would be the same as the instant application. Arnold et al. do not teach a kit comprising said hybrid recombinase.

Sarkis et al. teach a mutant serine recombinase Tn3 resolvase, a mutation at position G101, wherein the mutation is G101S a mutant serine recombinase Tn3 resolvase, and further comprising a mutation Q105L, having one or more mutations at the 2,3 interface R2A and E56K. Sarkis et al. also teach additional mutations at positions including E124Q, D102Y, M103I, as well as catalytic domain and DNA binding domain. The catalytic domain of Sarkis et al. and the instant application is the same. Therefore, the length (amino acid 1-148) of the catalytic domain (claims 31-35) of Sarkis et al. would be the same as the instant application. Sarkis et al. do not teach a kit comprising said hybrid recombinase.

Pati et al. teach a recombinase and a kit comprising said recombinase.

By combining the teachings of Arnold et al., Sarkis et al. and Pati et al. it would have been obvious to one of ordinary skill in the art at the time of the invention was made to make a kit as taught by Pati et al. by using the polypeptide of Arnold et al. and Sarkis et al. for convenience for the user.

One of ordinary skill in the art would have been motivated to make a kit for easy to use, and convenience for the user.

One of ordinary skill in the art would have a reasonable expectation of success because making a kit by using recombinase enzyme is well known and widely used in the art.

Therefore, claims 67 would have been prima *facie* obvious to use one of ordinary skill in the art.

Conclusion

Status of the claims:

Claims 1-69 are pending.

Claims 5-6, 15-17, 24-27, 43-45, 48-51, 60-66 and 69 are withdrawn.

Claims 1-4, 7-14, 18-23, 28-42, 46-47, 52-59, 67-68 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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